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DEPARTMENT OF COMMERCE

National Institute of Standards and Technology

[Docket No.: 120104006-2006-01]

Identification of Human Cell Lines Project

AGENCY: National Institute of Standards and Technology, Commerce

ACTION: Notice.

SUMMARY: The National Institute of Standards and Technology (NIST) Biochemical Science Division announces its intent to identify by short tandem repeat (STR) profiling up to 1500 human cell line samples as part of the Identification of Human Cell Lines Project. All data and corresponding information will be posted in a publically held database at the National Center For Biotechnology Information (NCBI).

DATES: On the first of each month beginning after [INSERT DATE OF PUBLICATION] NIST will post the number of cell lines accepted on the NIST Applied Genetics Group website at http://www.nist.gov/mml/biochemical/genetics/index.cfm. Once the total number

of accepted submissions has reached 1400 cell lines, the next month will be the final month NIST will accept submissions, with the total time for acceptance not to exceed one year beyond [INSERT DATE OF PUBLICATION].

ADDRESSES: Hard copies of submissions must be submitted to the attention of Margaret Kline at the National Institute of Standards and Technology; 100 Bureau Drive, Stop 8314; Gaithersburg, MD 20899-8314. Electronic submissions must be submitted to Margaret.Kline@nist.gov.

FOR FURTHER INFORMATION CONTACT: Margaret Kline via e-mail at Margaret.Kline@nist.gov or telephone 301–975–3134.

SUPPLEMENTARY INFORMATION:

Program Description: The National Institute of Standards and Technology (NIST) Biochemical Science Division announces its intent to unambiguously identify by short tandem repeat (STR) profiling up to 1500 human cell line samples as part of the Identification of Human Cell Lines Project. All data and corresponding information will be posted in a publically held database.

The use of misidentified cell lines in cancer and other biomedical research continues to occur, resulting in the possibility that a significant proportion of the literature describing studies employing cell lines may be misleading or even false. The end result of this

unfortunate situation is that millions of dollars may be spent on research using misidentified cell lines every year worldwide. This, in turn, may delay discoveries and the effective translation of research findings from the laboratory to the clinic or the market. Scientists may believe or claim that they are working with cells derived from one individual or animal species, only to eventually learn that the cells were derived from a different individual or species. With the advent of standardized, simple, and rapid methods for human cell line authentication the identity of a cell line need no longer be in doubt. NIST is undertaking this project to provide that cell line authentication.

Human cell lines submitted for identification as part of this project will undergo STR profiling, a DNA profiling method that examines/screens for STRs (DNA elements 2-6 bps long repeated in tandem) in the human chromosomes, that has been shown to be not only rapid and inexpensive, but also able to generate reproducible data in a format suitable for use in a standard reference database. STR analysis involves simultaneous amplification of eight STR markers (e.g., D5S818, D13S317, D7S820, D16S539. vWA, THO1, TPOX, CSF1PO) and the amelogenin gene for gender determination. For each STR marker used, the power of discrimination improves by about an order of magnitude. Thus, with 8 STRs, random match probabilities on the order of 1 in 100 million are expected between cell line DNA samples originating from unrelated individuals. Each unique human cell line has a distinct DNA profile and when the STR DNA fragment sizes are converted to numeric values, the DNA profiles are readily compared among different laboratories. It should be noted, however, that STR profiling cannot detect interspecies cross-contamination. For this reason, cell lines grown on non-human feeder cells will not be accepted for this project.

The attributes of STR-profiling which have driven the selection of this technology over other possible candidates for this project include: (i) the ability to discriminate human cell lines to the individual level upon evaluating a relatively limited number of allelic markers; (ii) reproducibility of the endpoint across different laboratories and therefore the feasibility of assembling and maintaining a searchable and public (freely accessible) database for authenticating established cell lines; (iii) the commercial availability of STR-profiling kits, allowing individual laboratories to bring this technology in-house; (iv) relatively low cost; (v) rapidity; and (vi) reduced need for specialized technical expertise and/or reagents, compared with many of the other authentication technologies. Presently, cell line STR profiling appears to represent the greatest value to the scientific community for authenticating human cell lines unambiguously, quickly, and for the least expense.

There is a tremendous need for scientific researchers using cell lines to know with confidence that the cells they are using are of the desired origin. This interactive database will be used by the research and development community to validate cell lines of interest. The database will offer DNA profiles of commonly used standard cell lines, primary, differentiating, and commonly used immortalized and transformed cell lines, as donated by interested parties.

Furthermore, the database will allow disparate laboratories to compare their lines, thereby facilitating the validation of experimental data. Thus, the database will address the need for investigators to know much more about the samples used in their research, and will fulfill an

overarching need of researchers to characterize their substrates with an accepted standard.

The current databases for cell lines generated using various numbers of STR loci will be useful as long as the new extended set of STR loci include the current loci. Thus, the current database will not be absolute and can be updated when existing cell lines are retyped as a routine measure using the extended set of STR loci.

Information on cell lines in the database will include multiple attributes of the cell lines (name and possible synonyms of cell line, organism, tissue of origin, morphology, pathologic or disease-state, hybrid or mixed culture, feeder cells, date of origin, etc), the STR markers and procedures used in identification, the submitter and appropriate links, other descriptive material, and the STR profile (electropherogram) of the cell line.

Scientists at NIST will evaluate data from STR profiling as described in *Designation: ASN-0002 Authentication of Human Cell Lines: Standardization of STR Profiling* by. NIST will make no conclusions regarding uniqueness of cell line, whether the cell line matches another cell line, whether the cell line is misidentified, cross-contaminated, or genetically unstable.

Identification by STR profiling of human cell lines will be provided by the Biochemical Science Division (BSD)/Material Measurement Laboratory (MML)/NIST. This program is contingent upon the availability of BSD/MML/NIST program funds, BSD/MML/NIST program objectives, and the discretion of BSD/MML/NIST advisors. The timeline for completing the STR profiling will be contingent on resources available.

NIST anticipates entering into a Materials Transfer Agreement with each submitter. To obtain a copy of the NIST Materials Transfer Agreement to be used for this project, please contact Margaret Kline, whose contact information is given in the ADDRESSES section above.

Applicants who submit complete information about their cell lines and who enter into a Material Transfer Agreement with NIST will be eligible to participate in the Identification of Human Cell Lines Project on a first-come, first served basis. Once the Material Transfer Agreement is executed, institutions will have 30 business days to submit the agreed-upon cell lines. Note that submitters must be willing to have submitter information made public in the aforementioned database.

Submission Process: Submitters should contact Margaret Kline with a list of proposed cell lines for identification. Each submitter may submit up to 15 cell lines. Note that no cell lines grown on non-human feeder cells will be accepted due to the possibility of contamination. NIST will perform STR profiling of up to 1500 cell lines submitted with complete information on a first-come, first-serve basis. As part of the submission, the following information, using standard nomenclature, should be included for each cell line or DNA extract, as applicable. Please do not include any personally identifiable information regarding the source of the cell lines.

Submitter
Name:

Title:
Department:
Institution:
Institution Address:
Phone number:
Fax number:
Email:

Originator
Name:
Title:
Department:
Institution:
Institution Address:
Phone number:
Fax number:
Email:

Generic Information:
Cell Line Name =
Organism =
Tissue of Origin =
Morphology =
Pathologic or Disease-State =
Hybrid or Mixed Culture =

Specialized Information
Feeder Cells (species):
Passage Number:
Population Doubling Level (PDL):
Complete Growth Media:
Date of Origin/Date Established:
Reference:

If DNA extracts are submitted, the following information is required:
Source of DNA:
Cell line or derivatives
Fresh biopsy/tissue
Frozen biopsy/tissue
OCT-treated tissue
FFPE-treated tissue

DNA Isolation Method:
Organic (phenol/chloroform)
Salting-out

Other (Cellmark kit)

Method of DNA Quantitation:
PicoGreen
Spectrophotometer (Nanodrop, etc.)
PCR
Syber Green
Other (qRT-PCR)

Amount of DNA Used for Analysis:
Other Characterization and Authentication Methods: (example: cytogenetic analysis i.e. G-banding or SKY; Microarray analysis; SNP; isoenzymology)
Other Characterization and Authentication Methods: provide reference and data
Are the cell lines genetically engineered? If yes, explain how.

Costs for shipping accepted cell lines to NIST are the responsibility of the donating party, and will not be paid for by NIST.

Review and Selection Process: All submissions will be reviewed to determine whether they are complete. All complete submissions will be accepted based on date and time of receipt of submission. Up to 15 cell lines per submitter or establishment will be accepted, with a final limit of 1500 cell lines. No cell lines grown on non-human feeder cells will be accepted due to the possibility of cross-species contamination.

Research Projects Involving Human Subjects, Human Tissue, Data or Recordings

Involving Human Subjects: NIST has determined that this project does not include research involving human subjects that falls under the Common Rule for the Protection of Human Subjects.

Paperwork Reduction Act: **This notice contains collection of information requirements subject to the Paperwork Reduction Act (PRA). The collection of information has been approved by OMB under control number 0693-0064, and completion of this information for a single cell line is expected to take 2 hours and 30 minutes. Notwithstanding any other provision of the law, no person is required to respond to, nor shall any person be subject to a penalty for failure to comply with, a collection of information, subject to the requirements of the PRA, unless that collection of information displays a currently valid OMB Control Number.**

Dated: January 27, 2012

Willie E. May
Associate Director for Laboratory Programs

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